IFW

Docket No.: 4705-0117PUS1
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Ogari PACHECO et al.

Application No.: 10/566,466 | Confirmation No.: N/A

Filed: January 31, 2006 | Art Unit: N/A

For: STABLE PHARMACEUTICAL COMPOSITION OF FLUOROETHER COMPOUND FOR ANESTHETIC USE, METHOD FOR STABILIZING A FLUOROETHER COMPOUND, USE OF STABILIZER AGENT FOR PRECLUDING THE DEGRADATION OF A FLUOROETHER COMPOUND

Examiner: Not Yet Assigned

LETTER

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Subsequent to the filing of the above-identified application on January 31, 2006, attached hereto is an English translation of the International Preliminary Examination Report (Form PCT/IPEA/409) that should be made of record in the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or to credit any overpayment to Deposit Account No. 02-2448 for any

additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Dated: April 20, 2006

Respectfully submitted,

By _____

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Attachment(s)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
PI0303489-5		
International application No.	International filing date (*day/month/year*)	Priority Date (*day/month/year*)
PCT/BR 2004/000156	20 August 2004 (20.08.2004)	10 September 2003 (10.09.2003)

International Patent Classification (IPC) or national classification and IPC

IPC[8]: ***A61K 31/075*** (2006.01); ***A61K 9/00*** (2006.01)

Applicant

CRISTALIA PRODUTOS QUIMICOS FARMACEUTICOS LTDA.

1. This international preliminary examination report has been prepared by this International Preliminary Examination Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 3 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 5 sheets.

3. This report contains indications relating to the following items:

   - I. ☒ Basis of the opinion
   - II. ☐ Priority
   - III. ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV. ☐ Lack of unity of invention
   - V. ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI. ☐ Certain documents cited
   - VII. ☐ Certain defects in the international application
   - VIII. ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
07.03.2005	24 February 2006 (24.02.2006)
Name and mailing address of the IPEA/AT Austrian Patent Office Dresdner Straße 87 A-1200 Vienna Facsimile No. 1/53424/200	Authorized officer KRENN M. Telephone No. 1/53424/435

Form PCT/IPEA/409 (cover sheet) (July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/BR 2004/000156

I. Basis of the report

1. With regard to the **elements** of the international application:*

☐ the international application as originally filed

☒ the description:
pages 1-28, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____.

☒ the claims:
pages _____, as originally filed
pages _____, as amended (together with any statement) under Article 19
pages _____, filed with the demand
pages 36-40, filed with the letter of 6 December 2005 (06.12.2005).

☒ the drawings:
pages 1-7, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____.

☐ the sequence listing part of the description:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____.

☐ the claims, Nos. _____.

☐ the drawings, sheets/fig _____.

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as „originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/BR 2004/000156

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 1-31	YES
	Claims ----	NO
Inventive step (IS)	Claims 1-31	YES
	Claims ----	NO
Industrial applicability (IA)	Claims 1-31	YES
	Claims ----	NO

Citations and explanations (Rule 70.7)

Both WO 2003/030862 A2 and WO 2003/018102 A2 describe fluoroether compositions wherein the solvent is a polyalcohol, e.g. propylene glycol or polyethylene glycol (= $H(OCH_2CH_2)_nOH$, wherein n is at least 4). As said documents neither specifies the amounts of the stabilizer nor mentions menthol as stabilizer, claims 1-31 are new. After amendment of the claims also inventiveness is now given for all claims.

The state of the art is represented by WO 1998/032430 A1 and WO 1999/034762 A1. Whereas the first document discloses Lewis acid inhibitors, e.g. water and thymol (= aromatic compound), as stabilizers of fluoroether compositions, the latter shows a container constructed from a material containing polypropylene resp. polyethylene resins for storing fluorether compounds.

Industrial applicability is given.

AMENDED CLAIMS

We claim:

1. Stable pharmaceutical composition, characterized by comprising an amount of a fluoroether anesthetic compound selected from the group constituted of sevoflurane, desflurane, isoflurane, enflurane and methoxyflurane, and at least one stabilizer agent employed in a concentration ranging from 0.001% to 5% in weight of the final composition, being the stabilizer agent a polyalcohol selected from the group constituted of propylene glycol, polyethylene glycol, hexylene glycol, 1,3-butyleneglycol, or a C_1-C_6 alkyl substituted or unsubstituted aliphatic 4-12 membered carbocyclic alcohol like menthol, or mixtures thereof.

2. Stable anesthetic pharmaceutical composition characterized by comprising an amount of sevoflurane and at least one stabilizer agent, employed in a concentration ranging from 0.001% to 5% in weight of the final composition, being the stabilizer agent a polyalcohol selected from the group constituted of propylene glycol, polyethylene glycol, hexylene glycol, 1,3-butyleneglycol, or a C_1-C_6 alkyl substituted or unsubstituted aliphatic 4-12 membered carbocyclic alcohol like menthol, or mixtures thereof.

3. Stable anesthetic pharmaceutical composition according to claim 2 wherein the stabilizing agent is propylene glycol employed in a concentration ranging from 0.001% to 0.200% in weight of the final composition.

4. Stable anesthetic pharmaceutical composition according to claim 2 wherein the stabilizer agent is a polyethylene glycol of general formula $H(OCH_2CH_2)_nOH$ where n is equal or greater than 4 employed in a concentration ranging from 0.001% to 0.200% in weight of the final composition.

5. Stable anesthetic pharmaceutical composition according to claim 4 wherein the stabilizer agent is polyethylene glycol 400.

6. Stable anesthetic pharmaceutical composition according to claim 2 wherein the stabilizing agent is menthol.

7. Stable anesthetic pharmaceutical composition according to claim 6 wherein menthol is used in a concentration ranging from 0.001% to 0.200% in weight of the final composition.

8. Stable anesthetic pharmaceutical composition characterized by comprising an amount of sevoflurane and propylene glycol in a concentration ranging from 0.005% to 0.100% in weight of the final composition.

9. Stable anesthetic pharmaceutical composition characterized by comprising an amount of sevoflurane and polyethylene glycol 400 in a concentration ranging from 0.005% to 0.100% in weight of the final composition.

10. Stable anesthetic pharmaceutical composition characterized by comprising an amount of sevoflurane and menthol in a concentration ranging from 0.005% to 0.100% in weight of the final composition.

11. Method for stabilizing sevoflurane characterized by using at least one stabilizer agent in a concentration ranging from 0.001% to 5% in weight in relation to the weight of sevoflurane, being the stabilizer agent a polyalcohol selected from the group constituted of propylene glycol, polyethylene glycol, hexyleneglycol, 1,3-butyleneglycol, or a C_1-C_6 alkyl substituted or unsubstituted aliphatic 4-12 membered carbocyclic alcohol like menthol, or mixtures thereof.

12. Method according to claim 11 wherein the stabilizer agent is propylene glycol employed in a concentration

ranging from 0.001% to 0.200% in weight in relation to the weight of sevoflurane.

13. Method according to claim 11 wherein the stabilizer agent is a polyethylene glycol of general formula $H(OCH_2CH_2)_nOH$ where n is equal or greater than 4 employed in a concentration ranging from 0.001% to 0.200% in weight in relation to the weight of sevoflurane.

14. Method according to claim 13 wherein the stabilizer agent is polyethylene glycol 400.

15. Method according to claim 11 wherein the stabilizer agent is menthol employed in a concentration ranging from 0.001% to 0.200% in weight in relation to the weight of sevoflurane.

16. Method for stabilizing anhydrous fluoroether compounds characterized by using at least one stabilizer agent employed in a concentration ranging from 0.001% to 5% in weight in relation to the weight of the fluoroether compound, being the stabilizer agent a polyalcohol selected from the group constituted of propylene glycol, polyethylene glycol, hexylene glycol, 1,3-butylene glycol, or a C_1-C_6 alkyl substituted or unsubstituted aliphatic 4-12 membered carbocyclic alcohol like menthol.

17. Method according to claim 16 wherein the stabilizer agent is propylene glycol.

18. Method according to claim 17 wherein propylene glycol is used in a concentration ranging from 0.001% to 0.200% in weight in relation to the fluoroether compound.

19. Method according to claim 16 wherein the stabilizer agent is a polyethylene glycol of general formula $H(OCH_2CH_2)_nOH$ where n is equal or greater than 4.

20. Method according to claim 19 wherein the stabilizer agent is polyethylene glycol 400.

21. Method according to claim 20 wherein polyethylene glycol 400 is used in a concentration ranging from 0.001% to 0.200% in weight in relation to the fluoroether compound.

22. Method according to claim 16 wherein menthol is used in a concentration ranging from 0.001% to 0.200% in weight in relation to the fluoroether compound.

23. Method according to claim 16 wherein the anhydrous fluoroether compound is sevoflurane.

24. Method for stabilizing a fluoroether compound presenting water content from 0.002% to 0.14% characterized by using at least one stabilizer agent employed in a concentration ranging from 0.001% to 5% in weight in relation to the fluoroether compound being the stabilizer a polyalcohol selected from the group constituted of propylene glycol, polyethylene glycol, hexylene glycol, 1,3-butylene glycol, or a C_1-C_6 alkyl substituted or unsubstituted aliphatic 4-12 membered carbocyclic alcohol like menthol.

25. Method according to claim 24 wherein the stabilizer agent is propylene glycol.

26. Method according to claim 25 wherein propylene glycol is used in a concentration ranging from 0.001% to 0.200% in weight in relation to the fluoroether compound.

27. Method according to claim 24 wherein the stabilizer agent is a polyethylene glycol of general formula $H(OCH_2CH_2)_nOH$ where n is equal or greater than 4.

28. Method according to claim 27 wherein the stabilizer agent is polyethylene glycol 400.

29. Method according to claim 28 wherein polyethylene glycol 400 is used in a concentration ranging from 0.001% to 0.200% in weight in relation to the fluoroether compound.

30. Method according to claim 24 wherein menthol is used in a concentration ranging from 0.001% to 0.200% in weight in relation to the fluoroether compound.

31. Method according to claim 24 wherein the fluoroether compound presenting water content ranging from 0.002% to 0.14% is sevoflurane.